

Supporting Text

Note on R^2 values. All of the models of neuronal activity tested in this experiment returned relatively low R^2 values. The best performing model returned R^2 values that were typically below 0.4. However, these low R^2 values should not be interpreted as weak statistical support for the models. The expected R^2 values will depend to some extent on the design of the experiment.

To illustrate this point, imagine recording from a visually responsive neuron in V1 that responds well to a line segment and is tuned to orientation, direction of motion, speed, length of stimulus, the eye through which the stimulus is presented, and the luminance contrast of the stimulus. Imagine testing the neuron with a set of stimuli that vary only in orientation. No other stimulus attribute is varied. Under this condition, the firing rate of the neuron will vary from trial to trial, and the variance will be largely attributable to the orientation of the stimulus. A regression against orientation should return a high R^2 value, perhaps as high as 90%. This is because all other sources of variance have been minimized. Such an experiment asks whether orientation tuning, when isolated, is statistically reliable.

However, now imagine testing the neuron with a stimulus set in which all parameters are free to vary. From trial to trial, the stimulus changes in orientation, direction of motion, speed, length, the eye through which the stimulus is presented, and luminance contrast. The firing rate of the neuron will vary from trial to trial, but now the variance will arise from many sources. A regression against orientation should return a low R^2 value, perhaps in the 20–40% range, because orientation will account for only one part of the total variance. This seemingly low R^2 value, however, would not indicate a lack of orientation tuning, or a minimal or unimportant orientation tuning. Rather, it would indicate that orientation tuning accounts for a piece of the total variance, and that other factors must account for the remainder of the variance. One would expect the regression on orientation, even with a “low” R^2 of 0.2, to be highly statistically significant. This experimental design asks, in a varied stimulus set, (i) whether orientation tuning makes a

statistically significant contribution, and (ii) what proportion of the total variance of the neuron stems from orientation tuning.

In the same manner, in the present experiment we tested (i) whether each model of motor tuning made a statistically significant contribution to the pattern of firing of the neuron, and (ii) how much of the total variance of the neuron stemmed from each model. For example, one neuron, when tested on the end-posture-tuning model, returned an R^2 value of 0.38. The regression was highly significant ($P < 0.0001$). In this example, (i) end-posture tuning made a significant contribution to the behavior of the neuron, and (ii) 38% of the variance in the neuron's firing could be attributed to end-posture tuning, whereas the remainder of the variance must have been driven by other factors. Given the design of the experiment (the inclusion of an unrestricted, naturalistic movement set), such low R^2 values are expected. Particular attention, therefore, must be paid to the associated P value to ascertain the statistical significance of the fit.

Measurement of Joint Angles. The positions of points on the limb were measured by means of an Optotrak 3020 system (Northern Digital). This system tracks the 3D position of infrared light emitting diodes (LEDs). Each LED could be separately tracked to a spatial resolution of 0.1 mm. The position was measured every 14.3 ms. To create a marker that could be detected by the Optotrak cameras from any angle, we glued five individual LEDs together to produce an omni-directional marker ball. A marker ball was taped to the monkey's forefinger on the dorsal surface where it would not interfere with grasping; on the thumb, again on the dorsal surface where it would not interfere with grasping; on the back of the hand, between the knuckles of the third and fourth digits; and on the lateral aspect of the elbow. In addition, 14 individual markers were taped in a double ring around the monkey's wrist, with seven markers per ring and a 1-cm spacing between the rings. The wires were taped in a bundle to the underside of the arm and draped behind the monkey. The primate chair was open at the front and side, allowing for almost total range of movement of the arm. The monkey's other arm, ipsilateral to the electrode, was not studied with Optotrak markers. To ensure that this hand would not

reach for the fruit rewards during trials, or tear off the markers taped to the measured hand, this untested hand was fixed to the side of the chair in an arm holder.

The double ring of 14 markers around the wrist was subject to a rigid body computation to calculate the location and spatial orientation of the wrist. In this computation, for each time point, a 3D rigid model of the double ring of markers was fitted to the measured positions of the currently visible markers, using a least-squares method of optimal fit. The orientation and position of the model could then be used to estimate the orientation and center of the wrist. The center of the wrist was taken to be the mean position of the 14 points in the model.

The position of the shoulder in space was calculated by analyzing the position of the elbow over time. Over many time points, the elbow described a portion of a sphere, the origin of which was located at the shoulder joint. For each 3 min block of data, a shoulder position was calculated by fitting a sphere to the data using a least-squares best fit algorithm and using the center of the sphere as the shoulder location. Because the shoulder is capable of small translational movements in addition to rotations, this method of estimating shoulder joint location is approximate but was sufficient for the purposes of this study. When the shoulder position was calculated multiple times over different time segments, it varied within <3 cm.

Three shoulder angles were computed: the elevation; the azimuth; and the “twist” or internal/external rotation of the shoulder joint. We also calculated the flexion of the elbow; the pronation of the forearm; the extension of the wrist; the adduction of the wrist; and the grip aperture. In total, eight degrees of freedom were calculated for the arm. This model of the arm was verified by applying forward kinematics to estimate the position of the hand. This calculated position of the hand matched the actual, measured position of the hand to within an accuracy of 1.5 cm.

Description of Movements in the Data Set. During testing of a neuron the monkey was allowed to move its contralateral arm freely to touch and explore parts of the primate

chair, to reach for small pieces of fruit held out on the end of forceps, to bring food to its mouth, to retrieve food from its mouth, to hold food in central space to examine it, and to rotate and explore food items. Occasionally the monkey also scratched at its skin or scratched rhythmically at a portion of the monkey chair. The movement of the arm was recorded through all of these behaviors. Different types of behaviors were not separated in the analysis, partly because one type of behavior tended to grade into another type and the distinction could only be made subjectively; and partly because the purpose of the study was to include all possible arm movements in as large and naturalistic a range as possible given the constraints of the primate chair.

For each neuron, the position of the hand in 3D space was tracked during a continuous time interval ranging from 10 to 30 min. Separate movements were extracted from this data set on the basis of a velocity analysis. Minima in the velocity were identified and the intervals between minima were flagged as potential separate movements. To enter the final data set, the movement had to be at least 0.15 sec in duration and the peak speed had to be at least 20 cm per sec. These parameters seemed to successfully divide the data into discrete segments that matched our subjective impression of separate hand movements.

Fig. 4 shows a typical movement set collected during testing of a neuron. This set shows 683 separated movement segments that densely sampled the workspace of the hand. Vertically, the movements ranged from 29 cm below the mouth to 9 cm above the mouth. Horizontally the movements ranged on the contralateral side (same side as the studied arm, opposite side as the electrode) to 19 cm from the midline, and on the ipsilateral side to 13 cm from the midline. In depth (direction along the monkey's forward line of sight) the movements ranged from 5 cm behind the level of the mouth (such as when the monkey was reaching to its flank or to its ear) out to 21 cm in front of the mouth (normal for a fully extended reach).

The average length of a movement was 9 cm (SD 6.6). The average hand speed was 26.7 cm/sec (SD 13.5). Each movement had a peak speed, and the average peak speed among all movements was 46.2 cm/sec (SD 28.1).

For each movement we calculated a standard curvature metric, as follows. The straight-line distance between the start and end of the movement was found. The total path-length of the movement was found. The ratio of these two quantities provided a curvature metric in which 1.0 corresponds to no curvature and smaller numbers correspond to increasingly curved movements. The average curvature was 0.9 (SD 0.08), indicating that the movements tended to be straight. In the figure, some movements appear to be highly curved. This appearance is a result of collapsing a 3D movement into a 2D depiction in which the long axis of the movement is not fully shown.

The distribution of movement directions was examined. For each movement we calculated a direction by connecting the start point to the end point and obtaining the azimuth and elevation angles. These directions were then plotted on a sphere. The directions appeared to be relatively evenly distributed. The sphere was divided into 20 equal sectors, and the movement directions were distributed over these 20 sectors with all sectors represented.

Preliminary Analysis of Neurons. To further specify the somatotopic portion of motor cortex that was studied, we performed a preliminary analysis on each neuron. Using a step-wise regression, we obtained the degree of correlation between the neuronal activity and the velocity of each of the eight measured joints. If we were recording primarily in a distal representation, we would expect to find significant regressions with distal joints including hand aperture, wrist flexion, wrist adduction, and forearm pronation. If we were recording primarily in a proximal representation, we would expect to find significant regressions with proximal joints including elbow flexion and the three degrees of shoulder rotation. Given the known overlap in motor cortex somatotopy, we expected to find intermingled neurons related to both proximal and distal joints. The results indicated that 89% of the neurons were significantly related to the proximal joints and 67% were significantly related to the distal joints. These results indicate that the studied neurons were in the forelimb representation in a region that emphasized the proximal joints over the distal joints.

Direction Tuning. Each neuron was tested for direction tuning in the following manner. For each movement, we calculated a mean firing rate of the neuron (spikes per sec during the movement). Since the neuron was presumed to affect movement with a conduction latency and a latency caused by the inertia of the arm, we shifted the analysis window for the single neuron data with respect to the movement data by a specific temporal offset. The appropriate offset for each neuron was estimated from the electrical stimulation data from the same cortical site, and was the latency for the hand to move after onset of electrical stimulation. This latency was typically about 70 ms.

Each hand movement was assigned a direction in Cartesian space based on the vector connecting the beginning and end point of the movement. Firing rate was modeled as a function of the angular deviation ($\Delta\theta$) between this movement vector and a preferred direction.

$$\text{Firing rate} = A \cos (\Delta\theta) + B.$$

A regression analysis was used to find the optimal preferred direction and coefficients, following the method of Georgopoulos *et al.* (1). The regression analysis provided an R^2 value indicating how much of the variance in neuronal activity could be attributed to the direction-tuning model. The regression analysis also provided an F and P value indicating whether the data showed a statistically significant trend in the direction of the model.

End-Point Tuning. For this model of neuronal tuning all data concerning the direction or trajectory of the movement was discarded and only the end-point of the movement was considered. Firing rate was modeled as a Gaussian function of these end-points in Cartesian space. In the following equation, x_1 , x_2 , and x_3 refer to the three Cartesian coordinates of the end-point of the movement; P_1 , P_2 , and P_3 refer to the coordinates of the peak of the Gaussian; the standard deviations of the Gaussian around that peak are indicated by σ_1 , σ_2 , and σ_3 ; the height of the Gaussian at peak is given by A ; and the height of the Gaussian at lowest, or the estimated baseline firing rate of the neuron, is B .

A nonlinear regression technique (2) was used to fit this equation to the data for each neuron.

$$\text{Firing rate} = Ae^{\frac{(x_1 - P_1)^2}{2\sigma_1^2} + \frac{(x_2 - P_2)^2}{2\sigma_2^2} + \frac{(x_3 - P_3)^2}{2\sigma_3^2}} + B$$

End-Posture Tuning. This model followed the same general equation as the previous model except that it involved the eight dimensions of arm posture space (x_1 through x_8) rather than the three dimensions of Cartesian space. Firing rate was modeled as a Gaussian function that had a peak at a specific, preferred posture. Again a non-linear regression technique was used to fit the model to the data for each neuron.

$$\text{Firing rate} = Ae^{\sum_{i=1:8} \frac{(x_i - P_i)^2}{2\sigma_i^2}} + B$$

End-Posture Plus Trajectory. This model added a term to the end-posture model. The movement of the arm through posture space was assigned an 8D vector that connected the beginning posture to the end posture of the movement. A second vector was defined connecting the beginning posture of the movement to the estimated preferred posture of the neuron. The angular deviation $\Delta\theta$ was defined as the difference in angle between these two vectors. In this model:

$$\text{Firing rate} = (C \cos(\Delta\theta) + D)(Ae^{\sum_{i=1:8} \frac{(x_i - P_i)^2}{2\sigma_i^2}} + B)$$

Testing Artificial Neurons. To test the validity of the above regression models, we generated artificial neurons. One artificial neuron was direction tuned. To generate the neuron we used the hand movements of an actual data set, but replaced the firing-rate data with artificially generated data. The data were generated using the direction-tuning

model, and then randomized noise was added to create a neuron that was noisily tuned to a preferred direction. The neuron was then subjected to the regression analyses described above. Fig. 5A shows the result. When tested with a direction-tuned model, the artificial direction tuned neuron showed a mid-range R^2 value consistent with its noisy tuning. When tested with the other regression models, it showed near zero R^2 values.

In a similar manner we generated an artificial neuron that was tuned to a final hand location in space, and an artificial neuron that was tuned to a final posture of the arm. The results, shown in Fig. 5 B and C, show that the R^2 value for each type of neuron was highest for the matching type of regression model and near zero for the non-matching regression models. These tests indicate that the regression models were successful at distinguishing neurons that had different types of tuning, with relatively little cross-contamination between the different regression models.

Distribution of Joint Angles Preferred by End-Posture-Tuned Neurons. For each neuron recorded from motor cortex, we used the end-posture regression model to obtain a Gaussian fit to the data in 8D posture space. We then examined the distribution of preferred end-postures among neurons. Not all neurons were sharply tuned in posture space. To examine the distribution of those neurons that had clear preferred postures, we ranked neurons by the sharpness of the Gaussian tuning function and arbitrarily chose the 50% of neurons that were most sharply peaked, thus the neurons for which the end posture was most clearly specified. These neurons are represented in Fig. 6. Each frequency histogram shows data for one joint. For most joints, neurons were tuned to a range of different preferred angles. For some joints, especially distal joints, neurons were more likely to be tuned to an extreme angle. Neurons tended to prefer a closed grip aperture.

1. Georgopoulos, A. P., Schwartz, A. B. & Kettner, R. E. (1986) *Science* **233**, 1416-1419.

2. Cohen, J., Cohen, P., West, S. G. & Aiken, L. S. (2003) *Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences* (Lawrence Erlbaum Associates, Mahwah, NJ), 3rd Ed.